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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,893	02/27/2006	Jean Pierre Plouet	0508-1134	2413

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YOUNG & THOMPSON
209 Madison Street
Suite 500
ALEXANDRIA, VA 22314

EXAMINER	
HADDAD, MAHER M	
ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,893	PLOUET ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-48* is/are pending in the application.

4a) Of the above claim(s) *27-35 and 37-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/11/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 27-48 are pending.

2. Applicant's election with traverse of Group V, claims 35-36 drawn to a process for preparing a monoclonal antibody that is capable of activating/inhibiting angiogenesis comprising the steps of: immunizing an animal by injection of cells with an angiogenic phenotype and the species of inhibiting angiogenesis, filed on 1/31/08, is acknowledged.

Applicant's traversal is on the grounds that given consideration and search has been performed on **all** the claims of the present invention (emphasis added) the prior Office Action, thus, there is no burden of search to continue to examine all the claims on the merits. This is not found persuasive because not all the claims were search in the prior Office action, only Groups I-II as indicated on page 4, top ¶ of the previous Office Action mailed on 11/20/07. Further evidence is shown by the applied art on the elected invention. Regarding the prior art of Nomura et al, the Examiner notes that Applicant is arguing limitations that are not claimed. However, in view of the newly applied art (see below) applicant's argument is moot. Accordingly, Applicant's inventions do not contribute a special technical feature when viewed over the prior art they do not have a single general inventive concept and so lack unity of invention as set forth in the previous Office Action and instant newly applied art.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 27-34, 37-48 (non elected Groups) and 35 (non-elected species), are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/31/08.

4. Claim 36 is under examination as they read on a process for preparing a monoclonal antibody that is capable of activating/inhibiting angiogenesis comprising the steps of: immunizing an animal by injection of cells with an angiogenic phenotype and the species of inhibiting angiogenesis.

5. Applicant's IDS, filed 4/11/05, is acknowledged, however, 2796073 document was crossed out because the English translation document was not found. Applicant is invited to produce such documents.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112.

> *The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.*

7. Claim 36 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitations "angiogenic phenotype" and "angiogenesis-inhibiting properties" claimed in claim 36 is ambiguous and indefinite. It is unclear what "phenotype" and "properties" of the angiogenesis are contemplated.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claim 36 is rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Pat. No. 6,440,733.

The US `733 patent teaches a process for preparing a monoclonal antibody recognizing an antigen on the surface of tumor vessel endothelial cells (an angiogenic phenotype) (col., 4, lines 17-20 in particular), wherein immunization can be accomplished by intraperitoneally administering living cells (10^6 to 10^7 cells) (without adjuvant) as an immunogen. The final immunization involves intravenous administration of 10^6 living cells (see col. 4, lines 42-46 in particular). The `733 patent further teaches that after said immunization, antibody-producing cells for preparing hybridomas are isolated from the immunized animal. Antibody-producing cells are preferably prepared with the spleen extracted from the immunized animal (see col., 5, lines 35-403 in particular). Then, thus obtained antibody-producing cells are immortalized by fusing them to myeloma cells (see col., 5, lines 44-47 in particular) using any cell fusion technique known to those skilled in the art may be used (see col., 5, lines 46-47 in particular). The `733 patent further teaches that the fused cells are selected by cultivation in a HAT medium, the cultivation of cells in the HAT medium may be done for a period enough to kill cells othere than hybridomas (see col., 6, lines 3-8 in particular). Further, cell line producing an intended antibody can be subcultured in ordinary media (see col., 6, lines 33-45 in particular). The `733 patent teaches that one of characteristics of monoclonal antibodies of the present invention is that the affinity for tumor vessel endothelial cells is comparable to or Higher than the affinity for normal vessel endothelial cells (see col. 6, lines 64-67 in particular). The `733 patent verifies that the resultant tumor vessel endothelial monoclonal antibodies have antiproliferative effect (angiogenesis-inhibiting properties) on tumor vessel endothelial cells (angiogenic cells) (see Example 5, col., 14 in particular).

The reference teachings anticipate the claimed invention.

10. Claim 36 is rejected under 35 U.S.C. 102(b) as being anticipated by Burrows et al (Clin Cancer Res. 1995 Dec;1(12):1623-34).

Burrows et al teach the use of subconfluent cultures of HUVECs which had previously been shown to secrete an angiogenic factor as an immunogen to generate monoclonal antibodies. HUVECs were harvested with a rubber policeman and 10^6 cells were injected i.p. into BALB/c

mice at 21-day intervals. Fusion with myeloma cells was performed. Hybndoma supernatants (numbering approximately 10,000) were screened for reactivity with proliferating HUVECs. Antibodies that bound to HUVECs in the ELISA were further tested for reactivity with HUVEC cell surface determinants by flow cytometry. Hybridomas secreting antibodies against HUVEC cell surface antigens were cloned and subsequently screened for lack of reactivity with quiescent HUVECs in frozen sections of human umbilical vein. A small panel of antibodies that reacted with proliferating but not with quiescent HUVECs were selected for further immunohistochemical characterization using a series of malignant and normal human tissues. One antibody. TEC- 11. was chosen for further study (see page 1624, under *Production of the TEC-1l Antibody* in particular). Burrows et al teach that increased binding of TEC-11 to tumor vasculature and to dividing as opposed to noncycling HUVECs *in vitro* suggests that endoglin is an endothelial cell proliferation-associated marker. A dgA immunotoxin prepared with TEC-l 1 was greater than 3000-fold more inhibitory to proliferating (verifying angiogenesis-inhibiting properties) *versus* confluent HUVEC cultures (see page 1624, 1st col., 1st full ¶ in particular). Finally, Burrows et al teach that TEC- 11 binding became up-regulated on vessels at approximately the stage at which breast tumors become invasive (new blood vessels formation, angiogenesis) (see page 1627, 2nd col., 1st full ¶ in particular).

The reference teachings anticipate the claimed invention.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B. O'Hara can be reached on (571) 272-0878. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

February 27, 2008

/Maher M. Haddad/
Primary Examiner,
Art Unit 1644